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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,160	03/01/2007	Mary Ellen Rybak	13566.105023	1564

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
12/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,160	RYBAK, MARY ELLEN	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18 and 21-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-18 and 21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06182008; 09172008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January June 18, 2008 has been entered.

Applicant's Response Dated June 18, 2004

2. Claims 1, 3-18 and 21-29 are pending. An action on the merits of claims 1, 3-18 and 21-29 is contained herein below.

3. The rejection of claims 1, 3-18 and 21-25 under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa) is maintained for the reasons of record as set forth in the Office action mailed on March 20, 2008. Newly added claims 26-29 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa) as applied to claims 1, 3-18 and 21-25 in the Office action mailed on March 20, 2008.

Rejections of Record Set Forth in the Office Action Dated March 20, 2008

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1, 3-18 and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa).

Claims 1, 3-18 and 22-29 are drawn to a method of treating a human body having cancer comprising administering an effective therapeutic amount of ET-743 in combination with an effective therapeutic amount of a 5-fluorouracil pro-drug thereof. Claim 21 is drawn to a medical kit for administering ET-743 in combination with capecitabine.

Bowman teaches treating any mammal affected by cancer comprising administering a therapeutically effective amount of ET-743, or a pharmaceutical composition thereof (pages 7-8). Administration of the compounds is preferably by intravenous infusion. Infusion times of up to 72 hours are used. The correct dosage of the compound will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor being treated. Administration can be carried out continuously or periodically within the maximum tolerated dose. ET-743 may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time or a different time. Suitable candidates include antimetabolite drugs such as 5-fluorouracil.

Bowman differs from the instantly claimed invention in that Bowman does not teach the administration of capecitabine or other 5-fluorouracil pro-drugs; however, the use of capecitabine would have been obvious to one of ordinary skill in the art at the time of the invention.

Ishikawa teaches that cytotoxic anticancer drugs often cause severe side-effects because they do not act selectively in tumors. Capecitabine was designed to generate the active drug 5-FUra selectively in human tumors through three sequential steps of enzyme reactions in humans. Because these enzymes are so localized in the body, capecitabine is expected to generate 5-Fura selectively in tumor tissues, and consequently, to improve the efficacy and safety margins of 5-FUra, the parent drug.

It would have been obvious to one of ordinary skill in the art to use capecitabine. As taught by Ishikawa, capecitabine generates the active drug 5-FUra selectively and consequently, improves the efficacy and safety margins of the parent drug. Selection of appropriate dosage regimens will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor being treated, and such selection would have been well within the purview of the skilled artisan.

6. Applicant's arguments filed February 4, 2008 have been fully considered but they are not persuasive. Applicant argues that 1) the references fail to teach all of the claimed elements, and 2) the references fail to provide a reason for one of ordinary skill in the art to arrive at the claimed elements. Applicant further contends that not all combinations of an antitumoral drug with capecitabine are necessarily going to have acceptable tolerability in human patients.

Applicant's arguments are not persuasive. The Michaelson et al. reference cited by applicant has been noted; however, obviousness does not require absolute predictability. The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. Use of materials in combination, each of which is known to function for intended purpose, is generally held to be prima facie obvious as the idea of combining them flows logically from their having been individually taught in the prior art. In the instant case, Bowman teaches treating any mammal affected by cancer comprising administering a therapeutically effective amount of ET-743, or a pharmaceutical composition thereof (pages 7-8). Ishikawa teaches the use of capecitabine for the treatment of cancer. Thus, claims that require no more than the administration of two conventional anti-cancer compositions together in order to treat cancer in a patient set forth prima facie obvious subject matter. Furthermore, Bowman clearly suggests using ET743 in combination with other drugs for cancer treatment. See page 8 of Bowman.

Takahashi et al. and applicant's contention that the prior art teaches away from the instant invention have been noted; however, Ishikawa explicitly teaches the preference for using capecitabine over 5-fluorouracil and provides possible explanations for its superiority. Ishikawa teaches, "we concluded that capecitabine should be much safer and more effective than 5-FUra. In fact, capecitabine was much more effective at a wider dose range than 5-FUra in the human colon cancer xenograft models used in the present study." Selection of appropriate dosage regimens will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor

being treated, and such selection would have been well within the purview of the skilled artisan.

Conclusion

7. Claims 1, 3-18 and 21-29 are pending. Claims 1, 3-18 and 21-29 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patrick T. Lewis/
Primary Examiner, Art Unit 1623

/PL/